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EPIZOOTIC LYMPHADENITIS.*

A NEW DISEASE OF GUINEA-PIGS.

CHARLES H. BOXMEYER.

THIS disease of guinea-pigs otherwise known as "lumps" is characterized by swelling of the lymph glands (most frequently the anterior cervical group) which subsequently break down with the formation of large abscesses. These abscesses on attaining their full size perforate the overlying skin and discharge a large quantity of cheesy pus. The number of abscesses varies from one to ten or twelve. They are usually in different stages of development. Marked constitutional symptoms are absent. Death results from a terminal systemic infection or from pressure causes.

History.—The outbreak here described occurred in guinea-pigs reserved for breeding purposes in a caviery belonging to a western antitoxin manufacturer. Some 3,000 were in the loft, over half of which showed the disease when examined in February, 1904. Cases of "lumps" were first observed two years before the above date and steadily increased in numbers. At least 3,000 animals have been attacked.

How the disease first originated is unknown. Attempts to trace it to outside sources failed. It has since been controlled by the slaughter of all infected pigs and by careful cleansing and fumigation of the caviery. Occasional cases still appear, however, as many animals carry internal abscesses that escape detection.

Morbid anatomy.—Autopsies have been made on over 100 pigs of all sizes, most of which were killed for examination. The following are the post-mortem findings in a few typical cases:

Guinea-pig No. 090. Red and white male; weight, 600 grams; found dead July 10, 1905.

Three of the anterior cervical glands are transformed into abscesses 15, 20, 50 mm. in diameter respectively. These abscesses are but loosely attached to the adjacent structures. Each is inclosed in a thick capsule over which run dilated blood vessels. All are filled with a thick cheesy pus, yellowish white in color. The pleural cavity is filled with a thick opalescent fluid. Fibrin is deposited on the visceral pleura.

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Lungs compressed and congested.

A tumor originating in one of the mediastinal glands displaces the lungs downward and the heart to the left..

Pericardium is greatly distended by thick fluid containing large white flakes.

Liver congested. It shows subcapsular hemorrhages and nutmeg markings.

Spleen slightly enlarged. Kidneys show acute parenchymatous changes. The abdominal lymph glands are but slightly enlarged.

Guinea-pig No. 010. Female, weight 300 grams. Chloroformed August 5, 1905.

A cluster of four cherry-sized abscesses in the anterior cervical region. A large egg-sized cheesy gland in the left axilla.

Uterus shows in the left cornu a cherry-sized abscess. Other viscera normal.

Guinea-pig No. 030. Female, weight 500 grams. Chloroformed June 14, 1905.

Submental glands. Three enlarged to the size of beans. On section they show a moist glistening surface with several pin-head areas of softening at the periphery of the gland. In the left anterior cervical region is a 30 mm. incapsulated abscess. In front of this is a pear-shaped tumor (15×30 mm.) containing pus. The deep cervical glands are much enlarged and edematous. Viscera normal.

The neck glands are the most often affected, the anterior cervical, submental, or auricular glands in over 90 per cent of the animals examined. Next in frequency the axillary glands are involved, then the groin. Abscesses arising from a retro-peritoneal gland near the sacro-vertebral articulation are frequent. Large abscesses 30 mm. in diameter are found here closing the pelvic inlet. Abscess of the spleen was observed five times. In one case two abscesses were present, one pointing in the lateral abdominal wall. Abscesses of the mediastinal glands were found three times. The liver, the uterus, and the lungs were each involved once.

The development of the abscesses can best be followed by studying animals of different ages, since the infection takes place early in life and the tumors reach their full development in adults.

The cervical lymph glands of normal guinea-pigs are not palpable. In infected pigs, at the age of three or four weeks, the glands have swollen to the size of small peas and may be plainly felt as hard nodules beneath the skin of the neck. On autopsy the swollen edematous glands are seen lying in the more or less congested and edematous fascia. The glands show, on section, a moist, uniformly white surface. Areas of softening are not yet present.

In pigs weighing 250 to 300 grams the glands have reached the size of large beans and are for the greater part bean-shaped. Inflammatory changes in the surrounding tissue are not marked. On section the diseased glands appear much as in the smaller pigs, but in many, several small areas of softening are to be seen in the cortex.

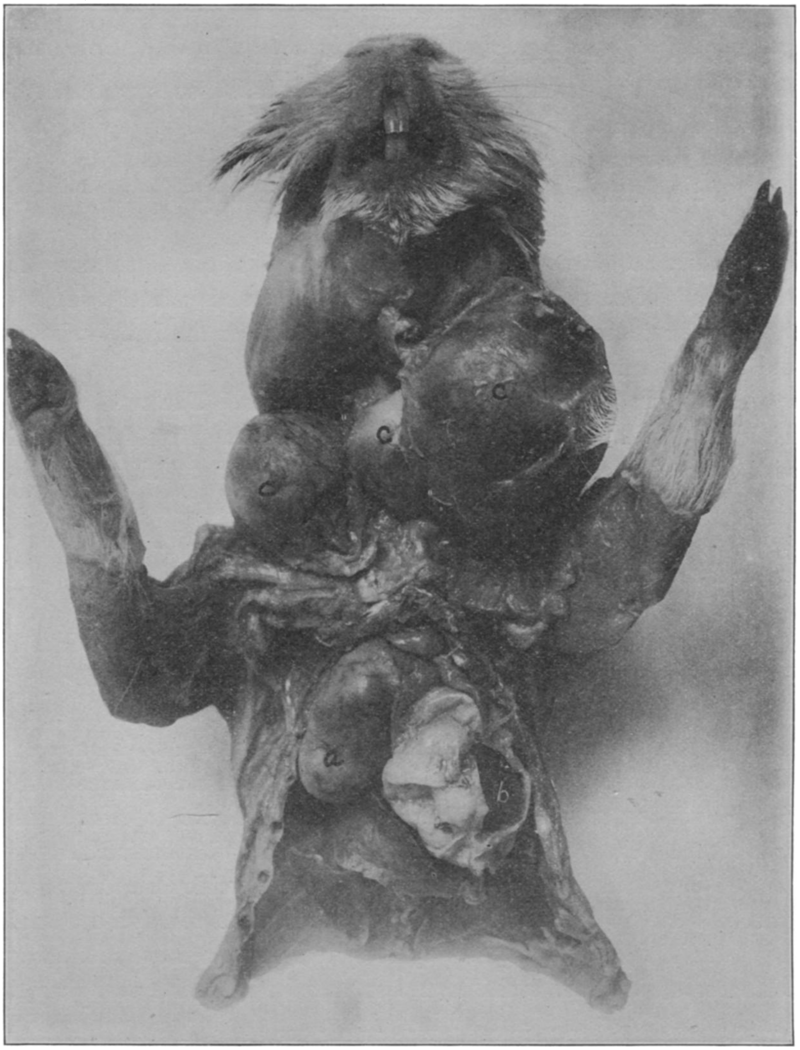

FIG. 1.—Photograph of Guinea-pig No. 090. Kaiserling preparation. *a*, Mediastinal gland; *b* heart; *c*, abscesses arising from cervical glands.

In older pigs these areas of softening increase in size and fuse. They become surrounded by a firm capsule. But one end of the gland may be broken down at this time into cheesy pus. From now on the growth of the tumors is rapid, the entire gland softens, the capsule thickens and becomes distended with pus. Large blood vessels are formed in the capsule and branch over its surface. The abscesses may reach the size of a hen's egg before rupturing through the skin. When the skin is perforated the pus is discharged and the abscess slowly heals by granulation. The pus is yellowish white and of the consistency of *Schmierkäse.*

Pigs dead of the disease show a general peritonitis, purulent pericarditis or pleuritis, or a pyemia.

Microscopic anatomy.—The lymph glands of pigs naturally infected or of inoculated animals which do not die acutely, show in the earliest stages of disease a marked dilation of the lymph sinuses and a desquamation of their endothelial cells. These cells have a ragged outline and show degenerative changes. The nucleus contains but very little chromatin and the cytoplasm stains faintly pink with eosin. These cells tend to collect in the cortical sinuses where they often fuse to multinucleated masses of considerable size.

While the germ centers show active proliferation, there is a marked decrease in the number of lymphocytes.

The capsule of the gland shows local proliferation. The peripheral lymph sinus is obliterated in these places and fibroblasts invade the cortex of the gland. At the same time, there is a development of large endothelial cells in the cortex and these with the fibroblasts form dense masses of large mononuclear cells. These cell groups form first, as a rule, in the spaces between the follicles of the gland involving them as they increase in size. The cytoplasm of the cells forming these masses stains deeply at first with basic dyes, but rapidly loses this power and acquires a slight acidophile character. The cells have large vesicular nuclei with small chromatin contents. A growth of fibroblasts tends very early to surround the mononuclear cell masses which are multiple and scattered around the periphery of the gland. There is a marked increase in the size of the lymph nodes due to this cell increase.

In later stages of the disease, polynuclear leucocytes appear in the centers of the cell collections. At times they are taken up by the mononuclear cells which are often completely filled with them.

From now on there is a rapid growth of the glands due to mononuclear increase and polynuclear infiltration. The foci soften in the center and pus is formed as in ordinary abscesses. Meanwhile, the fibroblasts form a capsule of increasing thickness around them. As the areas of softening approach each other, their individual capsules fuse more or less completely; a common capsule forming around them. This capsule thickens and becomes a true pyogenic membrane.

Microscopically the pus consists of polynuclear leucocytes and large mononuclear cells in various stages of disintegration. The large mononuclears are frequently loaded with cocci. Dense masses of necrotic cells are seen in the fluid portion of the pus.

Bacteriology.—In smears made from pus of the abscesses Gram staining cocci are always found either free or within the cells. They are generally present in large numbers, though many do not stain well. These organisms are usually seen as diplococci or short chains of four to six members, again as dense clumps or single cocci. These same cocci can almost always be found in smears and section made from the glands that have not yet begun to soften.

A large number of cultures have been made from about 200 animals. In every case a streptococcus has been obtained, in most instances in pure culture. The only other organism found has been a member of the hog-cholera group.[1] This organism has appeared in only a few cases and in these lesions characteristic of this group of organisms were present in the liver and spleen.

Except for some variations in virulence and fermentative power the streptococcus has apparently always been the same. As the virulence of the organism increases it tends to form longer chains in the animal body. In the peritoneal exudates occurring in terminal infections and in abscesses formed in very young pigs following inoculation with pus or cultures, it occurs as chains of considerable length.

The streptococcus in cultures occurs as chains of from 4 to 30 or more cocci somewhat variable in size. It is non-motile. No capsule has been seen. It stains well by Gram's method and with the ordinary stains.

Broth.—The growth is not very profuse. At the end of 24 hours the broth is perfectly clear. A considerable amount of white coarsely granular sediment is seen in the bottom of the tube. This soon subsides after shaking the tube. Under the microscope the sediment is seen to consist of tangled chains of streptococci.

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[1] SMITH AND STEWART, *Jour. Boston Soc. Med. Sci.*, 1897, p. 12.

Glucose broth.—The growth is more luxuriant than in plain broth. In fermentation tubes the greater development takes place in the closed branch, the growth adhering to the glass in filamentous masses. Acid, but no gas is formed.

Agar.—On the surface the growth occurs as minute colorless, usually discrete, circular colonies with entire margins and raised convex surface. The colonies show finely granular under the microscope. In moist media, chains and loops of streptococci are seen running out from the margins of the colonies. The color is yellowish white by reflected light and brownish by transmitted light. As the colonies increase in size they flatten. Stick cultures show minute globular colonies along the line of puncture.

Blood agar.—The colonies are identical in appearance with those on ordinary agar. A clear zone due to hemolysis of the red corpuscles surrounds each colony. The hemoglobin is not changed.

Löffler's blood serum.—This is the most favorable medium. Growth shows as minute dew-drop colonies usually more or less discrete. In very moist media the colonies may attain a diameter of 3 mm. The condensation water is clouded and contains a flocculent sediment.

Potato.—Minute globular pearl-like colonies appear. The condensation water is clouded heavily. Involution forms with marked variation in the size of the individuals forming the chain are seen.

Litmus milk.—Is rapidly reddened. Coagulation does not occur spontaneously in 10 days, but follows on heating old cultures.

Glucose and maltose serum waters are coagulated in 24 hours.

Lactose serum water is reddened. But the acid production is less than in milk.

Mannite is not fermented.

Susceptible animals.—The streptococcus of "lumps" is pathogenic for guinea-pigs, rabbits, and mice. It has not been tested on other animals. Mice and rabbits are apparently not infected spontaneously.[1]

Very young guinea-pigs are most susceptible. They die in from 1 to 30 days after inoculation with pus or cultures, from septicemia or pyemia. There is a marked local reaction and a swelling of the lymph glands in the region of the inoculation.

Subcutaneous and intraperitoneal injections lead to death in from 24 to 48 hours. Older pigs occasionally react only locally to subcutaneous inoculation.

A young rabbit inoculated with a culture by rubbing on the abraded skin of the ear, died in four and a half days. Autopsy showed a moderate local reaction and swelling of the cervical glands. Streptococci were recovered from the heart blood. An adult rabbit showed a slight local reaction to cutaneous inoculation.

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[1] Abscesses similar in appearance to those in guinea-pigs have been occasionally encountered in rabbits, but these contain pus of a different character and differ from "lumps" in their microscopic anatomy. These have always yielded cultures of an organism of the *B. mucosus capsulatus* type.

Subcutaneous injection of 0.5 c.c. in one rabbit and 0.1 c.c. into the ear vein of another caused death.

Mice have died after either cutaneous or subcutaneous inoculation from general sepsis.

Mode of infection.—Infection takes place as a rule early in the life of the animal. Adult animals show always cheesy glands and never the incipient stages alone. In addition, adult pigs are much less susceptible to experimental infection than the young.

TABLE.

No. Pig	White Cells	Per Cent Poly-nuclear	Per Cent Lymph-ocytes	Per Cent Large Mononuclear			Per Cent Eosin-ophile	Per Cent Mast Cells	
				Non-granular	Granular	Vacuole			
8...	12,400	52.0	25.2	12.0	5.3	0.6	4.3	0.6	
7...	12,400	45.0	29.7	16.0	5.3	2.0	1.0	1.0	
6...	14,600	75.0	15.0	8.0	1.0	0.7	0	0.3	
5...	13,500	40.4	45.0	12.7	1.6	0.3	0	0	
4...	12,400	42.0	46.0	....	10.0	...	1.7	0.3	
3...	14,800	50.3	43.2	....	6.4	...	0.1	0	8 normoblasts
2...	13,600	35.1	53.5	....	9.1	...	2.3	0	
1...	25,200	61.3	21.3	....	14.0	...	2.7	0.4	1 neutrophile myelocyte
10...	12,800	32.4	46.0	....	8.0	...	13.3	0.3	
9...	20,700	43.3	47.4	....	8.3	...	0.7	0.3	

The disease is without doubt a wound infection spread by the pus that escapes when abscesses rupture externally. The virus enters through small abrasions in the throat, in most cases caused by the rough food, e. g., oats, hay, etc. In proof of this, six guinea-pigs, weighing 300 grams each, were fed oats inoculated with a culture of streptococci. All showed temporary swelling of the cervical lymph glands, and one developed typical abscesses. Typical cervical abscesses have been repeatedly produced by rubbing culture or pus on the abraded skin of the ear. A healthy female who ate her artificially infected young showed three days later swelling of the cervical glands and 30 days afterward five or six enlarged cheesy cervical glands and a bean-sized gland in the left groin. The habit of biting each others' ears, which guinea-pigs have, explains the involvement of the auricular glands.

Infection follows the lymph stream. Inoculation on the forefoot leads to abscess of the axillary glands; on the hind foot, to abscess of the groin glands; on the ear, to the auricular and cervical glands.

The foregoing table gives the result of the examination of the blood of 10 adult guinea-pigs with cheesy glands. The red cells are unchanged from the normal in number and appearance.

Burnett[1] gives the normal number of leucocytes as 10,897 on the average, and the polynuclears as 31.52 per cent.

The findings then show a moderate leucocytosis and polynucleosis —a condition to be expected in an infection of this kind.

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[1] BURNETT, *Jour. Med. Res.*, 1904, 11, p. 537.